THE SYNTHESIS OF ETHYL 2-(2-CYANO-2-ETHOXYCARBONYL-ETHENYL)AMINO-3-DIMETHYLAMINOPROPENOATE. THE SYNTHESIS OF SUBSTITUTED AMINOAZOLO-, AMINOAZINO-PYRIMIDINONES AND 2*H*-1-BENZOPYRAN-2-ONES

Lovro Selič,[a] Simona Golič Grdadolnik,[b] and Branko Stanovnik [a,*]

[a] Faculty of Chemistry and Chemical Technology, University of Ljubljana, Aškerčeva 5, 1000 Ljubljana, Slovenia

[b] LO1, Department of NMR and Molecular Modeling, National Institute of Chemistry, Hajdrihova 19, POB 3440, 1001 Ljubljana, Slovenia

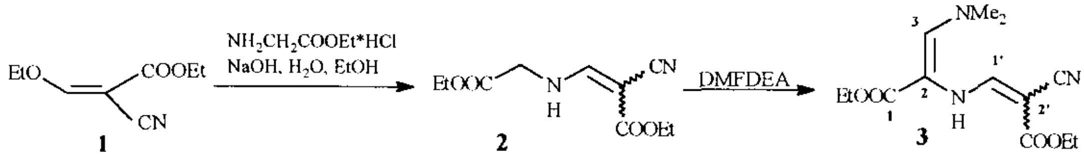
Dedicated to Dr. Bernhard Witkop on the occasion of his 80[th] birthday

Abstract - Ethyl 2-(2-cyano-2-ethoxycarbonylethenyl)amino-3-dimethylaminopropenoate (**3**) was prepared in two steps from ethyl 2-cyano-3-ethoxypropenoate, and used as a reagent for the preparation of *N*-protected 3-amino-4*H*-pyrido[1,2-*a*]pyrimidin-4-ones (**9a-c**), 5*H*-thiazolo[3,2-*a*]pyrimidin-5-one (**10**), 4*H*-pyrido[1,2-*a*]pyridin-4-one (**11**), 2*H*-1-benzopyranones (**12a**,**b**), and their tetrahydro derivatives (**13a**,**b**). Free amino 4*H*-pyrido[1,2-*a*]pyrimidin-4-ones (**14a-c**), 5*H*-thiazolo[3,2-*a*]pyrimidin-5-one (**15**) and 4*H*-pyrido[1,2-*a*]pyridin-4-one (**16**), were prepared from **9-13** by removal of the 2-cyano-2-ethoxycarbonylethenyl as *N*-protecting group by heating with hydrazine hydrate.

Recently, the synthesis of various derivatives of pyran-2-ones and fused pyran-2-ones has attracted an interest, since many of them have been found as nonpeptide HIV proteaze inhibitors.[1,2] Substituted 3-amino-4*H*-pyrido[1,2-*a*]pyrimidin-4-ones have been recently studied as candidate flourescent probes for hypoxic cells in solid tumors.[3] They have been prepared by condensation of substituted 2-aminopyridines with ethyl

3-ethoxy-2-nitropropenoate followed by cyclization in polyphosphoric acid, to give substituted 3-nitro-4*H*-pyrido[1,2-*a*]pyrimidin-4-ones. Reduction of the nitro group has been achieved using either titanium(III) chloride, Pd/C in the presence of hydrogen or cyclohexene by transfer hydrogenation in 53-82% yield.[4]
They have also been prepared by hydrolysis of the benzoylamino group of 3-benzoylamino-4*H*-pyrido[1,2-*a*]pyrimidin-4-ones in concentrated hydrochloric acid in yields below 30%.[5]
Recently, we have prepared a series of substituted alkyl 2-(2,2-disubstituted ethenyl)amino-3-dimethylaminopropenoates,[6-15] masked α-formyl-α-amino acid derivatives, as versatile reagents in the synthesis of many heterocyclic systems such as indolizines, quinolizines, pyranones, benzo- and naphtho-pyranones, pyranopyrimidines, azolo- and azinopyrimidines, with a monosubstituted amino group at position 3 in the newly formed ring.[16]
On the other hand, we have also observed that 2,2-disubstituted ethenyl groups, such as 2-benzoyl-2-(ethoxycarbonyl)ethenyl and 2-benzoyl-2-(methoxycarbonyl)ethenyl groups can be applied as *N*-protecting groups in the synthesis of didehydropeptides containing *N*-terminal 3-heteroarylamino-2,3-didehydro-alanine moiety, since they can be easily removed with hydrazine or hydroxylamine under mild conditions.[17]
Similarly, 3-amino substituted fused pyrimidinones have been prepared in high yields.[8-10,12]
In this paper we present, as an extension of our research in this area, the synthesis of ethyl 2-(2-cyano-2-ethoxycarbonylethenyl)amino-3-dimethylaminopropenoate (**3**) and its application for the synthesis of fused pyrimidines and pyranones with an amino group attached at position 3 in the newly formed system.
Ethyl 2-(2-cyano-2-ethoxycarbonylethenyl)amino-3-dimethylaminopropenoate (**3**) was prepared in the following way: ethyl 2-cyano-3-ethoxypropenoate (**1**) was converted with ethyl glycinate hydrochloride in ethanol at room temperature to give ethyl *N*-(2-cyano-2ethoxycarbonylethenyl)glycinate (**2**) in 80% yield. This was treated with *N,N*-dimethylformamide diethyl acetal (DMFDEA) in acetonitrile to give **3** in 47% yield. (Scheme 1).

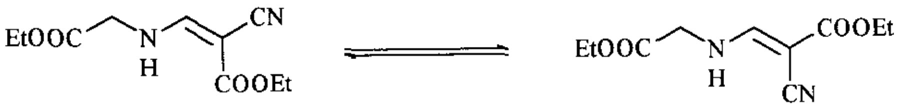
Scheme 1



The structure of **2** and **3** was determined by ^{1}H NMR spectroscopy. The chemical shift differences of the two sets of signals showed that compound (**2**) exists in solution in an equilibrium of **(*Z*)-2** and **(*E*)-2** isomers in ratio 1:1. (Scheme 2).

The most characteristical differrence was observed for NHCH structural element, at δ= 6.60 ppm (N*H*CH) and δ= 7.84 ppm (NHC*H*) with the coupling constant J_{CHNH}= 15.0 Hz for (*E*)-isomer and δ=9.10 ppm (N*H*CH) and δ= 7.28 ppm (NHC*H*) with the coupling constant J_{CHNH}= 13.7 Hz for (*Z*)-isomer.

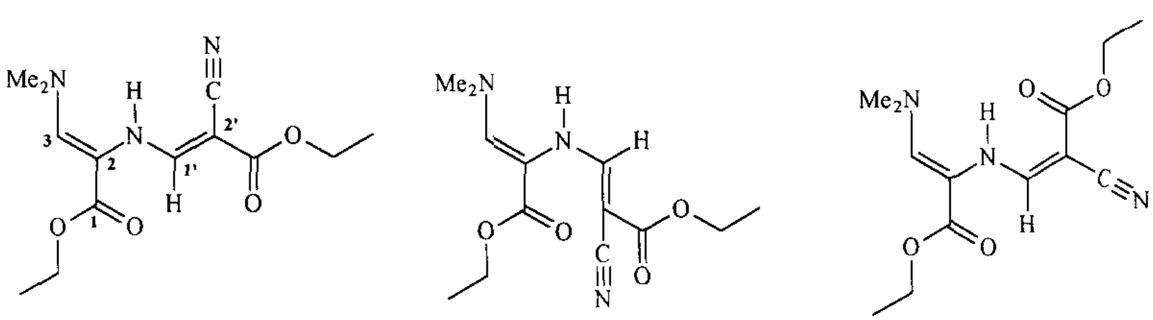
Scheme 2



(*Z*)-2 **(*E*)-2**

Compound (**3**) showed in the ^{1}H NMR three sets of signals. The most characteristic are three singlets for H_3 at δ= 7.25, 7.27 and 7.28 ppm, and three pairs of doublets for CHNH structural element at δ= 7.56, 7.60 and 7.79 ppm for CH part and at δ= 9.57, 9.30 and 9.22 ppm for the NH part, with the coupling constants J_{CHNH}= 14.05, 14.05 and 7.52 Hz, respectively. These data indicate that there are three isomers in equilibrium; two isomers having *anti* orientation of CHNH protons, while the orientation in the third isomer is *syn*. It has been shown that ^{13}C-^{1}H longe range coupling constants may be used in the configuration assignment of some trisubstituted alkenes. It has been successfully applied as a criterion for the *E,Z*-differentiation of ethyl 2-acyloxy-2-alkenoates[18] and NOESY, ROESY and HMBC techniques have been successfully employed for orientation of groups in 2,3-diaminopropenoates even if only one isomer is avaiable.[19]

Scheme 3

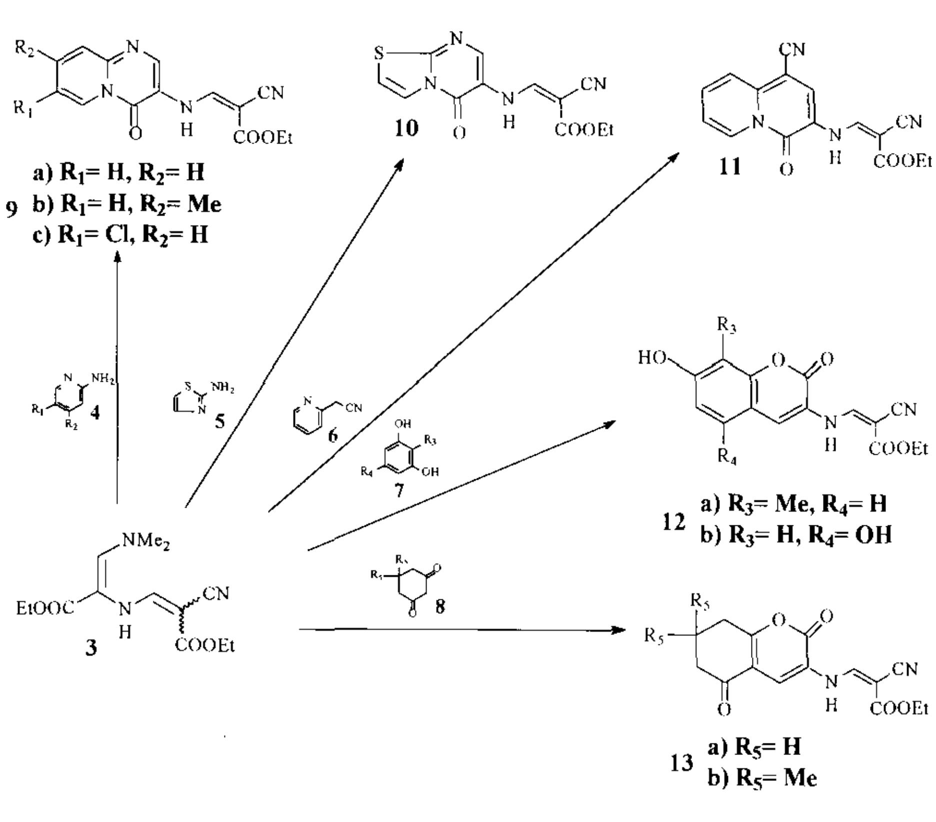


(3a) 43% anti (2*Z*,1'*E*) **(3b) 36% syn (2*Z*,1'*E*)** **(3c) 21% anti (2*Z*,1'*Z*)**

Since the assignment of isomers was not possible on the basis of ^{1}H NMR characteristics, the structures of isomers and the ratio among them was finally established by NOESY and chemical exchange techniques to be 43% *anti(2Z,1'E)* (**3a**), 36% *syn(2Z,1'E)* (**3b**), and 21% *anti(2Z,1'Z)* (**3c**). (Scheme 3).

The dimethylamino group in compound (**3**) can be formally substituted with *N*- and *C*-nucleophiles. The following *N*-nucleophiles were selected: 2-aminopyridine (**4a**), 2-amino-4-methylpyridine (**4b**), 2-amino-5-chloropyridine (**4c**), and 2-aminothiazole (**5**). They were treated with an equimolar amount of **3** in acetic acid under reflux. After 2.5 - 3 hours, derivatives of 4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**9**) and 5*H*-thiazolo-[3,2-*a*]pyrimidin-5-one (**10**) were isolated. (Sheme 4).

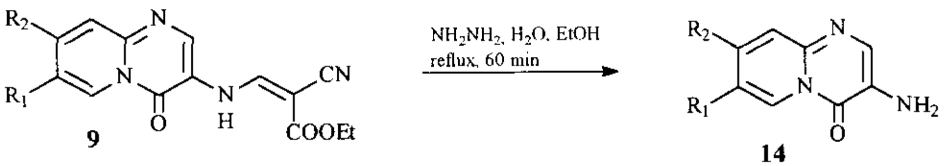
Scheme 4



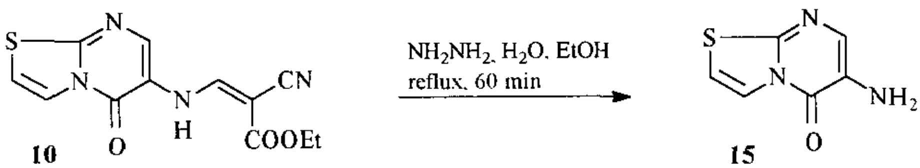
Two types of *C*-nucleophiles were used: 2-pyridylacetonitrile (**6**) was transformed with compound (**3**) in acetic acid into 4*H*-pyrido[1,2-*a*]pyridin-4-one derivative (**11**), while 2-methylbenzene-1,3-diol (**7a**), and benzene-1,3,5-triol (**7b**), and cyclic 1,3-diketones, such as cyclohexane-1,3-dione (**8a**) and dimedone (**8b**) gave 2*H*-1-benzopyran-2-one derivatives (**12**) and 5,6,7,8-tetrahydro-2*H*-1-benzopyran-2-one derivatives (**13**), respectively. (Scheme 4).

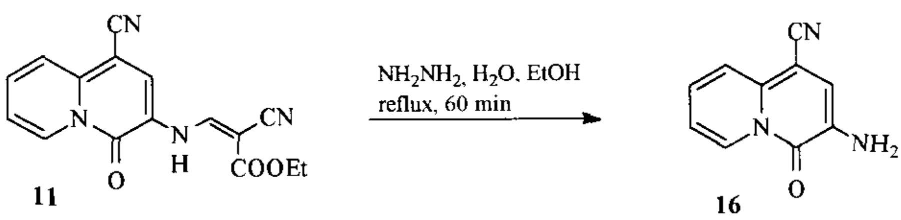
Removal of the 2-cyano-2-ethoxycarbonylethenyl group at the N^3 atom of compounds (**9** - **11**) was achieved by treatment with hydrazine hydrate in ethanol at reflux temperature to give the free amino compounds (**14** - **16**) in 45 - 98% yield, respectively. (Scheme 5).

Scheme 5



9,14	R1	R2	Yield (%)
a	H	H	45
b	H	Me	98
c	Cl	H	61





EXPERIMENTAL

Melting points were taken on a Kofler micro hot stage. The ^1H NMR spectra were obtained on a Bruker Avance DPX 300 spectrometer with TMS as the internal standard, IR spectra on a Perkin-Elmer 1310 or 727 B spectrophotometer and elemental analyses for C, H and N on a Perkin-Elmer CHN Analyser 240 C.

Ethyl *N*-(2-Cyano-2-ethoxycarbonylethenyl)glycinate (2). To a solution of ethyl glycinate hydrochloride (150 mmol, 20.94 g) in water (100 mL), sodium hydroxide (150 mmol, 6.00 g) was added. After sodium hydroxide was completely dissolved, ethyl 2-cyano-3-ethoxypropenoate (**1**, 150 mmol, 25.38 g) in ethanol (100 mL) was added to the stirred solution. Mixture was stirred for 1 h and then left overnight at -10° to -20°C. Precipitate was collected by filtration and recrystallized from ethanol to give **2** in 80% yield (27.15 g), (50% (*Z*)-configuration, 50% (*E*)-configuration), mp 116-118°C; IR 2210 cm^{-1} (CN); ^1H NMR ($CDCl_3$): δ 1.30 and 1.31 (t, $COOCH_2CH_3$), 4.07 (d, CH_2NH), 4.22 and 4.26 (q, $COOCH_2CH_3$), 6.60 (m, *E*-NH), 7.28 (d, *Z*-C*H*NH), 7.84 (d, *E*-C*H*NH), 9.10 (m, *Z*-NH); $J_{CHNH(E)}$= 15.0 Hz, $J_{CHNH(Z)}$= 13.7 Hz, J_{CH2CH3}= 7.0 Hz, J_{CH2NH}= 6.3 Hz. ^1H NMR (DMSO-d_6) δ 1.22 (t, 2x$COOCH_2CH_3$), 4.08-4.19 (m, 2x$COOCH_2CH_3$, CH_2NH), 7.74(d, *Z*-C*H*NH), 8.02 (d, *E*-C*H*NH), 8.64 (m, *E*-NH), 9.12 (m, *Z*-NH). *Anal.* Calcd for $C_{10}H_{14}N_2O_4$: C, 53.09; H, 6.24; N, 12.38. Found: C, 52.81; H, 6.15; N, 12.35.

Ethyl 2-(2-Cyano-2-ethoxycarbonylethenyl)amino-3-dimethylaminopropenopate (3). Ethyl *N*-(2-cyano-2-ethoxycarbonylethenyl)glycinate (**2**, 100 mmol, 22.62 g) and dimethylformamide diethyl acetal (DMFDEA, 240 mmol, 41 mL) in acetonitrile (50 mL) were heated at reflux for 4 h. Volatile components were evaporated *in vacuo* and ethanol (20 mL) was added for crystallization. Precipitate was collected by filtration and recrystallized from ethanol to give **3** in 47% yield (13.22 g), (3 isomers), mp 99-101°C; IR 2200 cm^{-1} (CN); ^1H NMR (DMSO-d_6): δ 1.17 and 1.20 (t, $COOCH_2CH_3$), 2.99 (s, Me_2N), 4.02-4.20 (2xq, 2x$COOCH_2CH_3$), 7.25 and 7.27 and 7.28 (s, H_3), CHNH pairs for three isomers: 7.56 and 9.57 (21%, J=14.05 Hz), 7.60 and 9.30 (43%, J=14.05 Hz), 7.79 and 9.22 (36%, J= 7.52 Hz); J_{CH2CH3}=7.0 Hz. *Anal.* Calcd for $C_{13}H_{19}N_3O_4$: C, 55.51; H, 6.81; N, 14.94. Found: C, 55.65; H, 7.12; N, 14.64.

General Procedure for Reactions of Compound (3) with Heteroaryl Amines and *C*-Nucleophiles. To a solution of heteroaryl amine (1 mmol) or *C*-nucleophile (1 mmol) in acetic acid (4 mL), equimolar amount of compound (**3**) (281 mg, 1 mmol) was added, and the mixture was heated under reflux for several hours. Reaction was followed by TLC (DC-Alufolien Kieselgel 60 F 254, 0.2 mm, E. Merck, and chloroform/methanol 10:1 as a solvent). After the reaction was completed, acetic acid was evaporated and the solid residue recrystallized from an appropriate solvent. The following compounds were prepared in this manner:

3-(2-Cyano-2-ethoxycarbonylethenyl)amino-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (9a). This compound was prepared from 2-aminopyridine (**4a**), 3 h of reflux, in 33% yield (67% (*Z*)-configuration), mp 233-235°C (from toluene); ^1H NMR (DMSO-d_6): δ 1.29 (t, $COOCH_2CH_3$), 4.26 (q, $COOCH_2CH_3$), 7.41 (dd,

H_7), 7.75 (dd, H_9), 7.89 (dd, H_8), 8.71 (d, C*H*NH), 8.84 (s, H_2), 8.94 (dd, H_6); J_{H6H7}= 6.8 Hz, J_{H8H9}= 8.9 Hz, J_{CH2CH3}= 7.1 Hz, J_{CHNH}= 13.5 Hz. *Anal.* Calcd for $C_{14}H_{12}N_4O_3$: C, 59.15; H, 4.26; N, 19.71. Found: C, 59.12; H, 4.11; N, 19.79.

8-Methyl-3-(2-cyano-2-ethoxycarbonylethenyl)amino-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (9b). This compound was prepared from 2-amino-4-methylpyridine (**4b**), 3 h of reflux, in 31% yield (67% (*Z*)-configuration), mp 263-264°C (from toluene); ^{1}H NMR (DMSO-d_6): δ 1.28 (t, $COOCH_2CH_3$), 2.47 (s, 8-Me), 4.25 (q, $COOCH_2CH_3$), 7.28 (dd, H_7), 7.57 (d, H_9), 8.67 (d, C*H*NH), 8.78 (s, H_2), 8.93 (d, H_6); 10.86 (d, NH); J_{H6H7}= 7.3 Hz, J_{H7H9}= 1.8 Hz, J_{CH2CH3}= 7.3 Hz, J_{CHNH}= 13.1 Hz. *Anal.* Calcd for $C_{15}H_{14}N_4O_3$: C, 60.40; H, 4.73; N, 18.78. Found: C, 60.51; H, 4.55; N, 18.98.

7-Chloro-3-(2-cyano-2-ethoxycarbonylethenyl)amino-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (9c). This compound was prepared from 2-amino-5-chloropyridine (**4c**), 3 h of reflux, in 55% yield (67% (*Z*)-configuration), mp 225-238°C (from toluene); ^{1}H NMR (DMSO-d_6): δ 1.29 (t, $COOCH_2CH_3$), 4.22 (q, $COOCH_2CH_3$), 7.76 (d, H_9), 7.92 (dd, H_8), 8.72 (d, C*H*NH), 8.84 (s, H_2), 9.01 (d, H_6), 10.86 (d, NH); J_{H6H8}= 2.2 Hz, J_{H8H9}= 9.5 Hz, J_{CH2CH3}= 7.1 Hz, J_{CHNH}= 14.0 Hz. *Anal.* Calcd for $C_{14}H_{11}N_4O_3Cl$: C, 52.76; H, 3.48; N, 17.58. Found: C, 52.52; H, 3.44; N, 17.29.

6-(2-Cyano-2-ethoxycarbonylethenyl)amino-5*H*-thiazolo[3,2-*a*]pyrimidin-5-one (10). This compound was prepared from 2-aminothiazole (**5**), 3 h of reflux, in 25% yield (67% (*Z*)-configuration), mp 242-243°C (from toluene); ^{1}H NMR (DMSO-d_6): δ 1.27 (t, $COOCH_2CH_3$), 4.24 (q, $COOCH_2CH_3$), 7.65 (d, H_2), 8.12 (d, H_3), 8.52 (s, H_7), 8.59 (d, C*H*NH), 10.69 (d, NH); J_{H2H3}= 4.9 Hz, J_{CH2CH3}= 7.1 Hz, J_{CHNH}= 13.9 Hz. *Anal.* Calcd. for $C_{12}H_{10}N_4O_3S$: C, 49.65; H, 3.47; N, 19.30. Found: C, 49.77; H, 3.37; N, 19.00.

1-Cyano-3-(2-cyano-2-ethoxycarbonylethenyl)amino-4*H*-pyrido[1,2-*a*]pyridin-4-one (11). This compound was prepared from 2-pyridylacetonitrile (**6**), 2.5 h of reflux, in 30% yield (85% (*Z*)-configuration, mp over 270°C (from mixture of DMF and ethanol); ^{1}H NMR (DMSO-d_6): δ 1.29 (t, $COOCH_2CH_3$), 4.26 (q, $COOCH_2CH_3$), 7.47 (dd, H_7), 7.86 (dd, H_8), 7.93 (d, H_9), 8.56 (s, H_2), 8.68 (d, C*H*NH), 9.06 (d, H_6), 11.00 (d, NH); J_{H6H7}= 7.2 Hz, J_{H8H9}= 8.5 Hz, J_{H8H7}= 6.7 Hz, J_{CH2CH3}= 7.1 Hz, J_{CHNH}= 13.9 Hz. *Anal.* Calcd for $C_{16}H_{12}N_4O_3$: C, 62.33; H, 3.92; N, 18.17. Found: C, 61.93; H, 3.62; N, 18.29.

7-Hydroxy-8-methyl-3-(2-cyano-2-ethoxycarbonylethenyl)amino-2*H*-1-benzopyran-2-one (12a). This compound was prepared from 2,6-dihydroxytoluene (**7a**), 3.5 h of reflux in 3% yield (82% (*Z*)-

configuration), mp over 270°C (from ethanol); ^{1}H NMR (DMSO-d_6): δ 1.28 (t, $COOCH_2CH_3$), 2.23 (s, 8-Me), 4.25 (q, $COOCH_2CH_3$), 6.92 (d, H_5), 7.29 (d, H_6), 8.13 (s, H_4), 8.56 (d, *CH*NH), 10.44 (bs, 7-OH), 10.73 (d, NH); J_{H5H6}= 8.3 Hz, J_{CH2CH3}= 7.2 Hz, J_{CHNH}= 13.9 Hz. *Anal.* Calcd for $C_{16}H_{14}N_2O_5 \cdot {}^1/_2H_2O$: C, 59.44; H, 4.68; N, 8.66. Found: C, 59.62; H, 4.45; N, 8.80.

5,7-Dihydroxy-3-(2-cyano-2-ethoxycarbonylethenyl)amino-2*H*-1-benzopyran-2-one (12b). This compound was prepared from 1,3,5-trihydroxybenzene (**7b**), 1 h of reflux in 44% yield (100% (*Z*)-configuration), mp over 270°C decomp (from mixture of DMF and ethanol); ^{1}H NMR (DMSO-d_6): δ 1.27 (t, $COOCH_2CH_3$), 4.21 (q, $COOCH_2CH_3$), 6.25 and 6.32 (2xd, H_6, H_8), 8,15 (s, H_4), 8.67 (d, *CH*NH), 10.36 (bs, 5-OH, 7-OH), 10.73 (d, NH); J_{H8H6}= 1.6 Hz, J_{CH2CH3}= 7.1 Hz, J_{CHNH}= 13.8 Hz. *Anal.* Calcd for $C_{15}H_{12}N_2O_6$: C, 56.97; H, 3.82; N, 8.86. Found: C, 56.71; H, 3.53; N, 9.01.

5-Oxo-3-(2-cyano-2-ethoxycarbonylethenyl)amino-5,6,7,8-tetrahydro-2*H*-1-benzopyran-2-one (13a). This compound was prepared from 1,3-cyclohexandione (**8a**), 2.5 h of reflux, in 46% yield (78% (*Z*)-configuration), mp 227-231°C (from toluene); ^{1}H NMR (DMSO-d_6): δ 1.27 (t, $COOCH_2CH_3$), 2.06 (t, CH_2), 2.52 (m, CH_2), 2.88 (t, CH_2), 4.24 (t, $COOCH_2CH_3$), 7.97 (s, H_4), 8.75 (d, *CH*NH), 10.68 (d, NH); J_{CH2CH2} = 6.1 Hz, J_{CH2CH3}= 7.1 Hz, J_{CHNH}= 13.6 Hz. *Anal.* Calcd for $C_{15}H_{14}N_2O_5$: C, 59.60; H, 4.67; N, 9.27. Found: C, 59.59; H, 4.51; N, 9.24.

7,7-Dimethyl-5-oxo-3-(2-cyano-2-ethoxycarbonylethenyl)amino-5,6,7,8-tetrahydro-2*H*-1-benzopyran-2-one (13b). This compound was prepared from 5,5-dimethyl-1,3-cyclohexandione (**8b**), 2.5 h of reflux, in 96% yield (78% (*Z*)-configuration), mp 234-235°C (from mixture of DMF and ethanol); ^{1}H NMR (DMSO-d_6): δ 1.07 (s, 2x7-Me), 1.27 (t, $COOCH_2CH_3$), 2.44 (s, CH_2), 2.81 (s, CH_2), 4.24 (q, $COOCH_2CH_3$), 7.96 (s, H_4), 8.76 (d, *CH*NH), 10.68 (d, NH); J_{CH2CH3}= 7.1 Hz, J_{CHNH}= 13.6 Hz. *Anal.* Calcd. for $C_{17}H_{18}N_2O_5$: C, 61.81; H, 5.49; N, 8.48. Found: C, 61.59; H, 5.44; N, 8.48.

General Procedure for Removal of the 2-Cyano-2-ethoxycarbonyl Group. To a starting compound (1 mmol), 0.5M solution of hydrazine hydrate in ethanol (4 mL), was added. The mixture was heated under reflux for 1 h. After that, mixture was cooled until precipitate was formed, which was further collected by filtration. Compounds were recovered in analytical pure form without further purification. The following compouds were prepared in this manner:

3-Amino-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (14a). This compound was prepared from **9a** (0.284 g, 1 mmol), in 45% yield; mp 176-178°C (from ethanol), (lit.,[5]: 180-182°C); ^{1}H NMR (DMSO-d6): δ 5.18 (s, NH_2), 7.10 (ddd, H_7), 7.40-7.52 (m, H_8, H_9), 7.91 (s, H_2), 8.73 (ddd, H_6), J_{H6H7} =7.3 Hz, J_{H8H9} =9.0 Hz, J_{H7H8} =5.6 Hz, J_{H6H8} =1.1 Hz, J_{H7H9} = 2.2 Hz, J_{H6H9} =0.6 Hz.

3-Amino-8-methyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (14b). This compound was prepared from **9b** (0.298 g, 1 mmol), in 98% yield; mp 225-226°C (from ethanol), (lit.,[20]: 215-225°C); ^{1}H NMR (DMSO-d6): δ 2.34 (s, 8-Me), 5.01 (s, NH_2), 6.97 (dd, H_7), 7.26 (d, H_9), 7.86 (s, H_2), 8.66 (d, H_6), J_{H6H7} = 7.2 Hz, J_{H7H9} = 1.9 Hz.

3-Amino-7-chloro-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (14c). This compound was prepared from **9c** (0.318 g, 1 mmol), in 61% yield; mp 192-193°C (from methanol), (lit.,[4]: 189-190°C); ^{1}H NMR (DMSO-d6): δ 5.42 (s, NH_2), 7.43 (dd, H_8), 7.49 (dd, H_9), 7.89 (s, H_2), 8.72 (dd, H_6), J_{H8H9} = 9.6 Hz, J_{H8H6} = 2.2 Hz, J_{H6H9} = 0.5Hz.

6-Amino-5*H*-thiazolo[3,2-*a*]pyrimidin-5-one (15). This compound was prepared from **10** (0.290 g, 1 mmol), in 72% yield; mp 169-172°C (from ethanol); ^{1}H NMR (DMSO-d6): δ 4.88 (s, NH_2), 7.42 (d, H_2), 7.52 (s, H_7), 7.90 (d, H_3); J_{H2H3} = 4.9 Hz. *Anal.* Calcd for $C_6H_5N_3OS$: C, 43.11; H, 3.01; N, 25.13. Found: C, 42.77; H, 3.13; N, 25.50.

3-Amino-1-cyano-4*H*-pyrido[1,2-*a*]pyridin-4-one (16). This compound was prepared from **11** (0.308 g, 1 mmol), in 85% yield; mp 202-204°C (from ethanol), (lit.,[11]:190-192°C); ^{1}H NMR (DMSO-d6): δ 5.63 (s, NH_2), 7.15 (dd, H_7), 7.22 (s, H_2), 7.38 (ddd, H_8), 7.64 (dd, H_9), 8.82 (dd, H_6); J_{H6H7} = 7.5 Hz, J_{H7H9} = 1.1 Hz, J, H_{6H8} = 1.1 Hz, J_{H8H9} = 9.0 Hz.

ACKNOWLEDGMENT

The authors wish to express their gratitude to the Ministry of Science and Technology, Slovenia, for financial support.

REFERENCES AND NOTES

1. L. Pochet, C. Doucet, M. Schynts, N. Thierry, N. Boggetto, B. Pirotte, K. Y. Jiang, B. Masereel, P. de Tullio, J. Delarge, and M. Reboud-Ravaux, *J. Med. Chem.*, **1996**, *39*, 2579; and references cited therein.
2. A. Mazumder, S. Wang, N. Neamati, M. Nicklaus, S. Sunder, J. Chen, G. W. A. Milne, W. G. Rice, T. R. Burke, Jr., and Y. Pommier, *J. Med. Chem.*, **1996**, *39*, 2472; and references cited therein.
3. J. Parrick and H. K. Rami, *J. Chem. Res. (S)*, **1990**, 308.
4. J. Parrick and H. K. Rami, *J. Chem. Res. (M)*, **1990**, 2411.
5. G. Horváth, I. Hermecz, A. Horváth, M. Pongor-Csákvári, L. Pusztay, A. I. Kiss, L. Czakó, and O. H. Abdirizak, *J. Heterocycl. Chem.*, **1985**, *22*, 481.
6. G. Soršak, A. Sinur, L. Golič, and B. Stanovnik, *J. Heterocycl. Chem.*, **1995**, *32*, 921.
7. R. Toplak, L. Selič, G. Soršak, and B. Stanovnik, *Heterocycles*, **1997**, *45*, 555.
8. L. Selič, S. Golič Grdadolnik, and B. Stanovnik, *Heterocycles*, **1997**, *45* (No. 12), in print.
9. L. Selič, S. Strah, R. Toplak, and B. Stanovnik, *Heterocycles*, **1998**, *47* (No. 2), in print.
10. L. Selič, S. Golič Grdadolnik, and B. Stanovnik, *Helv. Chim. Acta,* **1997**, *80*, in print.
11. S. Strah, B. Stanovnik, and S. Golič Grdadolnik, *J. Heterocycl. Chem.*, **1997**, *34*, 263.
12. S. Strah, A. Golobič, L. Golič, and B. Stanovnik, *J. Heterocycl. Chem.*, **1997**, *34*, in print.
13. G. Soršak, S. Golič Grdadolnik, and B. Stanovnik, *Bull. Soc. Chim. Belg.*, **1997**, *106*, in print.
14. M. Malešič, A. Golobič, L. Golič, and B. Stanovnik, *J. Heterocycl. Chem.*, in print.
15. L. Selič and B. Stanovnik, *J. Heterocycl. Chem.*, **1997**, *34*, 813.
16. For a review see: a) B. Stanovnik, *Molecules*, **1996**, *1*, 123; b) B. Stanovnik, *Methyl 2-Benzoylamino-3-dimethylaminopropenoate in the Synthesis of Heterocyclic Systems,* in *Progress of Heterocyclic Chemistry;* ed. by H. Sushitzky and E. F. V. Scriven, Pergamon Press, Oxford, **1993**, Vol. 5, pp. 34-53.
17. J. Svete, M. Aljaž-Rožič, and B. Stanovnik, *J. Heterocycl. Chem.,***1997**, *34*, 177.
18. P. Fischer, E. Schweizer, J. Langner, and U. Schmidt, *Magn. Reson. Chem.*, **1994**, *32*, 567.
19. S. Golič Grdadolnik and B. Stanovnik, *Magn. Reson. Chem.*, **1997**, *35*, 486.
20. J. Smodiš, B. Stanovnik, and M. Tišler, *J. Heterocycl. Chem.*, **1994**, *31*, 125.

Received, 17th November, 1997